

CLAIMS

1. A method of determining susceptibility to bone fracture in a subject, said method comprising analysing genetic material of a subject to determine the presence of the baT haplotype of the vitamin D receptor gene, wherein said haplotype is associated with risk of bone fracture.
2. A method of determining susceptibility to bone damage according to claim 1, said method comprising analysing the genetic material of a subject to determine which of the B/b, A/a and T/t alleles of the *BsmI*, *ApaI* and *TaqI* sites of the vitamin D receptor are present.
3. A method of determining susceptibility to bone fracture according to claim 1 or claim 2, said method further comprising analysing the genetic material of a subject to determine which allele of the collagen $\text{I}\alpha 1$ gene is present.
4. A method of determining susceptibility to bone fracture according to claim 3, said method comprising determining the presence of a G to T polymorphism at the *Sp1* site of the collagen $\alpha 11$ gene.
5. A method according to claims 1 to 4, wherein the haplotype may be determined by amplification of a relevant portion of the vitamin D receptor gene or collagen $\text{I}\alpha 1$ gene, followed by restriction enzyme digestion; or any other technique suitable for determining the genotype of a subject.
6. A method of determining susceptibility to bone fracture according to any one of the preceding claims, said method comprising determining the copy number of the B/b, A/a or T/t alleles of the vitamin D receptor gene and/or the S/s allele of the collagen $\text{I}\alpha 1$ gene.
7. A method according to any one of the preceding claims further comprising determining whether the allele(s) or haplotypes of the vitamin D receptor gene or collagen $\text{I}\alpha 1$ gene present is/are associated with risk of bone fracture.

AMENDMENT OF

16/10/00

8. A method according to claim 6 comprising comparing the allele(s) present in the genetic material of the subject with genotypes of the vitamin D receptor or collagen 1 α 1 genes having known degrees of risk of bone fracture.

9. A method according to any one of the preceding claims further comprising determining calcium levels in a subject.

10. A method according to claim 9 wherein daily calcium intake is measured.

11. A method according to any one of the preceding claims, wherein said method is performed *in vitro*.

12. A method according to claim 11 wherein said method is performed on blood, or tissue samples of a subject.

13. A method according to any one of the preceding claims further comprising treating the subject to reduce the risk of bone fracture.

14. A method according to claim 13, wherein suitable treatments include modifications to lifestyle, regular exercise, changes in diet or pharmaceutical preparations.

15. A method according to any one of the preceding claims wherein the subject is a mammal.

16. A method according to claim 15, wherein the subject is a human.

17. A method according to claim 15 or 16 wherein the subject is a female.

18. A method of predicting response of a subject to treatment, said method comprising analysing genetic material of a subject to determine the presence of the baT haplotype of the vitamin D receptor gene, wherein said haplotype is associated with risk of bone fracture.

19. A method according to claim 18, further comprising determining which allele(s) of the

AMENDMENT OF

1.6/12/20

Sub B9 collagen I α 1 gene is/are present.

20. A method according to claim 18, wherein said subject is diagnosed as being susceptible to bone fracture.

21. A method according to claims 18 or 19 further comprising administering the appropriate treatment.

Sub B10 22. Use of a kit to determine susceptibility to bone fracture in a subject, said kit comprising (i) one or more nucleic acid primer molecules for amplification of a portion of the vitamin D receptor gene, and (ii) means for determining whether the baT haplotype of said genes is present.

23. Use of a kit according to claim 22, further comprising (i) one or more nucleic acid primer molecules for amplification of a portion of the collagen I α 1 gene and (ii) means for determining which allele of said gene is present.

24. A kit for determining susceptibility to bone fracture in a subject, said kit comprising (i) one or more nucleic acid primer molecules for amplification of a portion of the vitamin D receptor gene, (ii) means for determining whether the baT haplotype of said gene is present; and (iii) means for indicating correlation between said allele(s) and risk of bone fracture.

25. A kit according to claim 24, said kit further comprising (i) one or more nucleic acid primer molecules for amplification of a portion of the collagen I α 1 gene and (ii) means for determining which allele of said gene is present.

26. A kit according to claim 24 or claim 25, said kit comprising DNA control samples, for comparison with DNA sequences of a subject.

add A9

Add A10

AMENDMENT OF

.....16/10/00.....